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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,121	06/13/2000	JEFFREY SCHLOM	2026-4266US1	9401

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EXAMINER
DECLOUX, AMY M

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application N . 09/529,121	Applicant(s) SCHLOM ET AL.	
	Examiner Amy M. DeCloux	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *20-45,49 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-19 and 46-48* is/are rejected.

7)☐ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-19 and newly added claims 46-48 in Paper No. 15, filed 2-28-02, is acknowledged. The traversal is on the ground(s) that the claims of the instant application share unity of invention with the peptide agonist being the common special technical feature of Groups I, III, IV and VI. This is not found persuasive because the unity of invention is broken upon the citation of prior art.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 20-45 and newly added claims 49-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 15.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

4. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). Applicant

should amend the first line of the specification to update the status (and relationship) of the priority documents. The first sentence of the specification should refer to the provisional application using language such as:

This application claims the benefit of U.S. Provisional Application No. 60/061,589, filed 10/10/97. See MPEP 1302.04.

Drawings

5. New formal drawings are required in this application, please see attached draftsman review Form PTO 892. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

Specification

6. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-5, 7-19 and 46-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide agonist of SEQ ID NO:1 consisting of the peptide SEQ ID NO:2, 3, 4 or 5, or a pharmaceutical composition thereof or a kit, wherein said sequences are an antagonist of the peptide consisting of SEQ ID NO:1's class I MHC HLA-A2 restricted T cell recognition, does not reasonably provide enablement for any other peptide agonist comprising any amino

acid substitution of any anchor position(s) of SEQ ID NO:1 with increased immungenicity, or a kit thereof or a pharmaceutical composition thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the large number of polypeptides broadly encompassed by the claims. The instant specification provides enablement only for peptides consisting of SEQ ID NO:s 2, 3, 4, or 5 that act as agonists of human CEA derived peptide consisting SEQ ID NO:1, wherein the agonist activity is defined in terms of their facilitation of the interaction between the MHC molecule and the T cell receptor (page 6 of the instant specification) . The instant specification discloses on page 6 that CEA is a cell surface antigen found in abundance on several types of cancer cells restricted by HLA-A2 MHC Class I molecules, and that the CEA agonistic peptides could be used in cancer immunotherapy. The specification discloses on page 35 that peptides consisting of SEQ ID NO:s 2, 3, 4, or 5 stimulate CEA specific CTL. Page 37 of the instant specification discloses that SEQ ID NO:2 can stimulate human CTL that are reactive with SEQ ID NO:1, which can then be used for adoptive transfer into humans.

However, the instant specification provides insufficient guidance and direction regarding peptides that comprise the peptides consisting of SEQ ID NO:2, 3, 4, or 5 which are all nonamers. Janeway et al (Immunobiology 4th Edition (1999) page 121) teach that CTLs recognize MHC class I peptides wherein said peptides are between 8-

10 amino acids long. Therefore one of skill would not be able to predict which amino acids could be added to the nonamers with the amino acid sequence of SEQ ID NO:2, 3, 4 or 5, such that said peptides retained their agonistic activity without additional guidance form the specification .

The instant specification discloses on page 35 that approximately 80 peptides were tested for their ability to act as agonists as defined above, but only 5 peptides were identified as agonists in a HLA-A2 restricted interaction. Therefore one of skill would not be able to predict which peptides comprising a peptide with one or more substitutions in non anchor positions of SEQ ID NO:1 would be agonistic activity without additional guidance form the specification.

The instant specification discloses on pages 24-25 that HLA-A2 is the only target employed and that the agonistic activity of a peptide consisting of SEQ ID NO:2 is not due to additional recruitment of another MHC class I molecule. The specification also discloses on page 29 that the T cells which recognized a peptide consisting of one of SEQ ID NO:2,3,4 or 5,were derived from humans with the HLA-A2 MHC haplotype. Janeway et al supra (page 121) teaches that the position and the identity of the anchors can vary depending on the particular MHC class I allele that is binding the peptide. Therefore it would require undue experimentation for one of skill to predict which non MHC anchor positions of SEQ ID NO:1 could be substituted without additional guidance form the specification because the non-anchor positions of peptides that bind different class I molecules can vary.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention

9. Claims 1-5, 7-19 and 46-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite a peptide comprising an agonist of SEQ ID NO:1. wherein the agonist has at least on amino acid substitution at a non-MHC anchor position of SEQ ID NO:1, a pharmaceutical composition thereof and a kit thereof.

However, the structure of said agonist is not adequately described for two reasons. First, only a partial structure is recited since the anchor positions can be any amino acid, including naturally occurring amino acids, and also non naturally occurring amino acids. Second, since the peptide comprises a nonamer, said peptide can also encompass an indeterminate number and type of additional amino acids, in addition to the recited nonamer. Since only a partial structure of the nonamer component of said peptide is recited, and since an indefinite number and type of additional amino acids may also be encompassed by the recited peptide, the agonist is not adequately described, especially given that the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify an agonist encompassed by the instant claims.

With the exception of the amino acid sequence of peptides consisting of SEQ ID NO:2,3,4 and 5), there is no description of the required structural and specific agonistic functional features of the recited agonist, or of the conserved regions that would be critical for these features. Further, the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the peptides encompassed (ie to distinguish agonists from antagonists) , with the exception of peptides consisting of SEQ ID NO:2,3,4 and 5. Therefore, the structure of a peptide comprising an agonist of SEQ ID NO:1, wherein the agonist has at least on amino acid substitution at a non-MHC anchor position of SEQ ID NO:1, a pharmaceutical composition thereof and a kit thereof, is not conventional in the art and one of skill in the art would not recognize from the disclosure that applicant was in possession of the genus of antagonists.

It is noted that though the claimed invention is directed to polypeptides and not cDNA, the principle of the following still holds for said polypeptides: a description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly&Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-5, 7-19 and 46-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claims 1-5, 7-19 and 46-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 and dependent claims 2-5 and 7-19 and 46-48 recites the broad recitation agonist, and the claim also recites “at least” which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Barnett,T., Goebel,S.J., Nothdurft,M.A. and Elting,J.J. Genomics 3 (1), 59-66 (1988) according to an NCBI blast search (of record, see restriction).

Said Blast search shows the 1988 submission by Barnett,T., Goebel,S.J., Nothdurft,M.A. and Elting,J.J. Genomics 3 (1), 59-66 (1988) of a CEA precursor protein which comprises the sequence YRSGENLNL at positions 249-257 . YRSGENLNL has at least one amino acid substitution at a non MHC anchor position 5. The instant specification discloses on page 33, that positions 2 and 9-10 are anchor positions and on page 34, lines 11-14 that position 5 is an a non-anchor amino acid by virtue of its positioning towards the TCR. Absent evidence to the contrary the peptide YRSGENLNL at positions 249-257 of CEA acts as an agonist of SEQ ID NO:1. Therefore, the referenced art anticipates the claimed invention.

Allowable Subject Matter

16. Claim 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy M. DeCloux whose telephone number is 703 306-5821. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703 308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are 703 305-3014 for regular communications and 703 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

Amy DeCloux, PhD
Patent Examiner, Group 1600
June 2, 2002
Amy DeCloux 6-3-02